

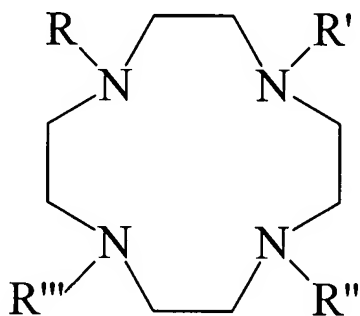
AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS::

1. (Currently amended) A contrast agent comprising:

a tetraazacyclododecane ligand having a general formula as follows:



wherein pendent arms R, R', R'' and R''' are amides having a general formula:

$-\text{CR}_1\text{H}-\text{CO}-\text{NH}-\text{CH}_2-\text{R}_2$, wherein R_1 includes organic substituents and R_2 is not

hydrogen; and

a paramagnetic metal ion coordinated to said tetraazacyclododecane ligand; and

a water molecule associated with said tetraazacyclododecane ligand and said

paramagnetic metal ion wherein said water molecule has a $\Delta\omega \cdot \tau_M \geq 1$ and a $\Delta\omega \geq 6$ ppm.

2. (Currently amended) The contrast agent as recited in Claim 1 wherein at least one said R_2 is selected from the group consisting of:

-COOEt;

-COO⁻;

-POOEt;

-PO₃⁻²;

pyridine; and

phenol further including a water molecule associated with said tetraazacyclododecane

~~ligand and said paramagnetic metal ion such that said water molecule has a $\Delta\omega \bullet \tau_M \geq 1$.~~

3. (Currently amended) The contrast agent as recited in Claim 1 2 wherein said R_2 on each of said pendent arms has the general formula: $-(CH_2)_nCOOR_4$ where

$n = 1-19$; and

R_4 is selected from the group consisting of:

H;

Group IA or IIA metal ions; and

alkyl groups containing from one to twenty Carbon atoms said $\Delta\omega \geq 6$ ppm.

4. (Currently amended) The contrast agent as recited in Claim 2 wherein said $\Delta\omega \geq 20$ ppm ~~$\tau_M \geq 1 \mu s$.~~

5. (Original) The contrast agent as recited in Claim 1 wherein said paramagnetic metal is selected from the group consisting of:

Eu³⁺;

Tb³⁺;

Dy³⁺; and

Ho³⁺.

6. (Original) The contrast agent as recited in Claim 1 wherein said paramagnetic metal is selected from the group consisting of:

Pr³⁺;

Nd³⁺;

Sm³⁺;

Er³⁺; and

Tm³⁺.

7. (Original) The contrast agent as recited in Claim 1 wherein said R₂ does not have a proton exchangeable group.

8. (Original) The contrast agent as recited in Claim 7 wherein said R₂ is selected from the group consisting of:

Alkyl groups having 20 carbon atoms or less;

Cycloalkyl groups having 20 carbon atoms or less;

Alkyloxy groups having 20 carbon atoms or less;

Alkyl ethers having 10 oxygen atoms or less and 20 carbon atoms or less; and

Polyols having 20 carbon atoms or less.

9. (Original) The contrast agent as recited in Claim 1 wherein said R₁ is selected from the group consisting of:

H;

Alkyl groups having 20 carbon atoms or less;

Cycloalkyl groups having 20 carbon atoms or less;

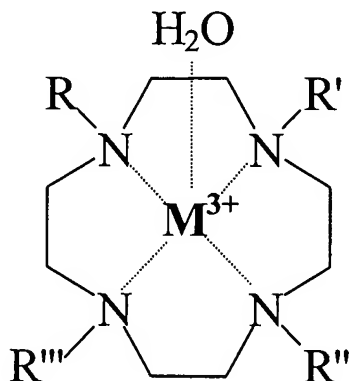
Alkyloxy groups having 20 carbon atoms or less;

Alkyl ethers having 10 oxygen atoms or less and 20 carbon atoms or less; and

Polyols having 20 carbon atoms or less.

10. (Currently amended) A method of using a magnetic resonance (MR) contrast agent, comprising:

subjecting a contrast agent contained within a sample to a radio frequency pulse wherein said contrast agent is a tetraazacyclododecane ligand having a general formula of:



wherein pendent arms R, R', R'' and R''' comprise organic substituents and said tetraazacyclododecane ligand further includes a paramagnetic metal ion (M^{3+}) coordinated to said tetraazacyclododecane ligand and a water molecule (H_2O) associated with said tetraazacyclododecane ligand wherein said water molecule has a $\Delta\omega \cdot \tau_M \geq 1$ and a $\Delta\omega \geq 6$ ppm; and

obtaining a magnetization transfer signal by applying a radio frequency pulse at a resonance frequency of said water molecule.

11. (Currently amended) The method as recited in Claim 10 wherein said ~~water molecule has a~~ $\Delta\omega \geq 20$ ppm ~~$\Delta\omega \cdot \tau_M \geq 1$~~ .

12. (Original) The method as recited in Claim 10 further includes producing a magnetization transfer magnetic resonance image from said magnetization transfer signal.

13. (Original) The method as recited in Claim 10 further includes applying said radio frequency pulse as a saturating pulse.

14. (Original) The method as recited in Claim 10 further includes said contrast agent with at least one pendent arm containing an amide group.

15. (Original) The method as recited in Claim 14 wherein said pendent arms are identical and have the general formula:

-CHR₁-CO-NR₂-R₃, wherein R₁, R₂ and R₃ comprise organic substituents.

16. (Currently Amended) The method as recited in Claim ~~15~~ 14 wherein said R₁ and R₂ are H, and R₃ has the general formula: -(CH₂)_nCOOR₄ where

n = 1-20; and

R₄ is selected from the group consisting of:

H;

Group IA or IIA metal ions; and

alkyl groups containing from one to twenty Carbon atoms.

17. (Original) The method as recited in Claim 14 wherein said paramagnetic metal ion is selected from the group consisting of:

Tb³⁺;

Dy³⁺; and

Ho³⁺.

18. (Original) The method as recited in Claim 14 wherein said paramagnetic metal ion is selected from the group consisting of:

Eu³⁺;

Pr³⁺; and

Nd³⁺.

19. (Original) The method as recited in Claim 14 wherein said R_1 and R_2 are H, and R_3 has the general formula: $-(CH_2)_nP(O)(OR_4OR_5)$ where

$n = 1-20$;

said R_4 is selected from the group consisting of:

H;

alkaline earth metal ions of Groups IA or IIA; and

alkyl groups containing one to twenty Carbon atoms;

and said R_5 is selected from the group consisting of:

H;

alkaline earth metal ions of Groups IA or IIA; and

alkyl groups containing one to twenty Carbon atoms.

20. (Original) The method as recited in Claim 14 wherein said R_1 and R_2 are H, and R_3 has the general formula: $-(CH_2)_nR_4$ where

$n = 1-20$; and

R_4 is selected from the group consisting of:

Pyridine (Py); and

Phenol (Ph).

21. (Original) The method as recited in Claim 14 wherein said pendent arms R and R'' are identical, said pendent arms R' and R''' are identical, and said pendent arms R' and R''' are not equal to said pendent arms R and R'' .

22. (Original) The method as recited in Claim 21 wherein

said pendent arms R and R'' have the general formula:

$-CR_1H-CO-NH-CH_2-R_2$; and

said pendent arms R' and R''' have the general formula:

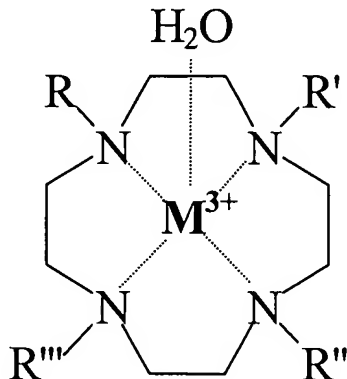


wherein said R₁, R₂, R₃, and R₄ comprise organic substituents; and R₂ is not equal to R₄.

23. (Original) The method as recited in Claim 14 further includes obtaining said magnetization transfer signal by applying a radio frequency pulse at a resonance frequency of said protons associated with said amide.

24. (Currently amended) A magnetic resonance system, comprising:

a magnetic resonance (MR) contrast agent, wherein said MR agent
tetraazacyclododecane ligand, having a general formula of:



wherein pendent arms R , R' , R'' and R''' comprise organic substituents and said tetraazacyclododecane ligand further includes a paramagnetic metal ion (M^{3+}) coordinated to said tetraazacyclododecane ligand and a water molecule (H_2O) associated with said tetraazacyclododecane ligand wherein said water molecule has a $\Delta\omega \cdot \tau_M \geq 1$ and a $\Delta\omega \geq 6$ ppm, and wherein said MR contrast agent produces a magnetization transfer signal when subjected to a radio frequency pulse; and

a magnetic resonance apparatus configured to produce said frequency pulse.

25. (Original) The magnetic resonance system recited in Claim 24, further comprising a sample containing said MR contrast agent.

26. (Original) The magnetic resonance system recited in Claim 24, wherein said sample is a living subject.

27. (Original) The magnetic resonance system recited in Claim 24, wherein said magnetic resonance apparatus produces a magnetization transfer image of said sample from said magnetization transfer signal.

28. (Original) The magnetic resonance system recited in Claim 27, wherein said magnetic resonance apparatus produces said magnetization transfer image by applying said radio frequency pulse at a resonance frequency of said water molecule.

29. (Original) The magnetic resonance system recited in Claim 28, wherein said magnetic resonance apparatus produces a magnetization transfer difference image by applying said radio frequency pulse at a $\Delta\omega$ of said water molecule, acquiring said magnetization transfer signal and subtracting said signal from a MR signal obtained by applying a radio frequency pulse at $-\Delta\omega$.

30. (Original) The magnetic resonance system recited in Claim 27, wherein said magnetic resonance apparatus produces said magnetization transfer image by applying said radio frequency pulse at a resonance frequency of protons associated with an amide included in one or more of said pendent arms.

31. (Original) The magnetic resonance system recited in Claim 24, wherein said radio frequency pulse is produced by said magnetic resonance apparatus and is a saturating pulse.

32. (Original) The magnetic resonance system recited in Claim 24, wherein said saturating pulse is applied at a resonance frequency of said water molecule.

33. (Original) The magnetic resonance system recited in Claim 24, wherein said saturating pulse ranges from about 1 to about 3 seconds.

34. (Currently amended) The magnetic resonance system recited in Claim 24 wherein said water molecule has a $\Delta\omega \bullet \tau_M \geq 4$.

35. (Original) The magnetic resonance system recited in Claim 24 wherein said $\Delta\omega \geq \underline{20}$ 6 ppm.

36. (Currently amended) The magnetic resonance system recited in Claim 24 wherein said $\Delta\omega \cdot \tau_M \geq 1$ occurs at a temperature of at least about 22°C ~~$\tau_M \geq 1$~~ μs .